PREDNISONE - prednisone tablet
PREDNISONE - prednisone solution
PREDNISONE - prednisone solution, concentrate
Roxane

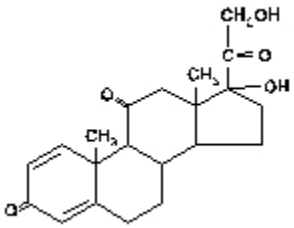
Rx only

DESCRIPTION

Each tablet contains:
Prednisone . . . . . 1, 2.5, 5, 10, 20, or 50 mg

Each 5 mL oral solution contains:
Prednisone . . . . . 5 mg
Alcohol 5%

Each mL *Intensol*™ contains:
Prednisone . . . . . 5 mg
Alcohol 30%
Prednisone is a glucocorticoid. Glucocorticoids are adrenocortical steroids, both naturally occurring and synthetic, which are readily absorbed from the gastrointestinal tract. The molecular formula for prednisone is $C_{21}H_{26}O_5$. Chemically, it is 17,21-dihydroxypregna-1,4-diene-3,11,20-trione and has the following structural formula:



Prednisone is a white to practically white, odorless, crystalline powder and has a molecular weight of 358.44. It melts at about 230°C with some decomposition. Prednisone is very slightly soluble in water; slightly soluble in alcohol, chloroform, dioxane, and methanol. Each tablet, for oral administration, contains 1, 2.5, 5, 10, 20, or 50 mg of prednisone. Prednisone Oral Solution contains 5 mg prednisone per 5 mL, and Prednisone Intensol contains 5 mg prednisone per mL.

Inactive Ingredients:
The tablets contain lactose, pregelatinized starch (corn), microcrystalline cellulose, sodium starch glycolate and magnesium stearate. The 1, 2.5 and 5 mg strengths also contain stearic acid.
The oral solution contains alcohol, citric acid, disodium edetate, fructose, hydrochloric acid, maltol, peppermint oil, polysorbate 80, propylene glycol, saccharin sodium, sodium benzoate, vanilla flavor and water. The Intensol™ contains alcohol, citric acid, poloxamer 188, propylene glycol and water.

CLINICAL PHARMACOLOGY
Naturally occurring glucocorticoids (hydrocortisone and cortisone), which also have salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states. Their synthetic analogs, such as prednisone, are primarily used for their potent anti-inflammatory effects in disorders of many organ systems.
Glucocorticoids, such as prednisone, cause profound and varied metabolic effects. In addition, they modify the body's immune responses to diverse stimuli.

INDICATIONS AND USAGE
Prednisone tablets and solutions are indicated in the following conditions:
1. *Endocrine disorders:*
   Primary or secondary adrenocortical insufficiency (hydrocortisone or cortisone is the first choice: synthetic analogs may be used in conjunction with mineralocorticoids where applicable; in infancy mineralocorticoid supplementation is of particular importance).
   Congenital adrenal hyperplasia
   Nonsuppurative thyroiditis
   Hypercalcemia associated with cancer

2. *Rheumatic disorders:*
   As adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in:

Psoriatic arthritis
Rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy)
Ankylosing spondylitis
Acute and subacute bursitis
Acute nonspecific tenosynovitis
Acute gouty arthritis
Post-traumatic osteoarthritis
Synovitis of osteoarthritis
Epicondylitis

3. *Collagen diseases:*
   During an exacerbation or as maintenance therapy in selected cases of:
   Systemic lupus erythematosus
   Acute rheumatic carditis

4. *Dermatologic diseases:*
   Pemphigus
   Bullous dermatitis herpetiformis
   Severe erythema multiforme (Stevens-Johnson syndrome)
   Exfoliative dermatitis
   Mycosis fungoides
   Severe psoriasis
   Severe seborrheic dermatitis

5. *Allergic states:*
   Control of severe or incapacitating allergic conditions intractable to adequate trials of conventional treatment:
   Seasonal or perennial allergic rhinitis
   Serum sickness
   Bronchial asthma
   Contact dermatitis
   Atopic dermatitis
   Drug hypersensitivity reactions

6. *Ophthalmic diseases:*
   Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as:
   Allergic conjunctivitis
   Keratitis
   Allergic corneal marginal ulcers
   Herpes zoster ophthalmicus
   Iritis and iridocyclitis
   Chorioretinitis
   Anterior segment inflammation
   Diffuse posterior uveitis and choroiditis
   Optic neuritis
   Sympathetic ophthalmia

7. *Respiratory diseases:*
   Symptomatic sarcoidosis
   Loeffler’s syndrome not manageable by other means
   Berylliosis
   Fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculous chemotherapy.
   Aspiration pneumonitis

8. *Hematologic disorders:*
   Idiopathic thrombocytopenic purpura in adults
   Secondary thrombocytopenia in adults
   Acquired (autoimmune) hemolytic anemia
   Erythroblastopenia (RBC anemia)
   Congenital (erythroid) hypoplastic anemia

9. *Neoplastic diseases*:

For palliative management of:
Leukemias and lymphomas in adults
Acute leukemia of childhood

10. *Edematous states:*
    To induce a diuresis or remission of proteinuria in the nephrotic syndrome, without uremia, of the idiopathic type or that due to lupus erythematosus.

11. *Gastrointestinal diseases:*
    To tide the patient over a critical period of the disease in:
    Ulcerative colitis
    Regional enteritis

12. *Miscellaneous:*
    Tuberculous meningitis with subarachnoid block or impending block when used concurrently with appropriate antituberculous chemotherapy.
    Trichinosis with neurologic or myocardial involvement.
    In addition to the above indications, prednisone is indicated for systemic dermatomyositis (polymyositis).

CONTRAINDICATIONS
Prednisone tablets and oral solutions are contraindicated in systemic fungal infections.

WARNINGS
In patients on corticosteroid therapy subjected to unusual stress, increased dosage of rapidly acting corticosteroids before, during, and after the stressful situation is indicated.
Corticosteroids may mask some signs of infection, and new infections may appear during their use. There may be decreased resistance and inability to localize infection when corticosteroids are used.
Prolonged use of corticosteroids may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerves, and may enhance the establishment of secondary ocular infections due to fungi or viruses.
Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium. These effects are less likely to occur with the synthetic derivatives except when used in large doses. Dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.
While on corticosteroid therapy patients should not be vaccinated against smallpox. Other immunization procedures should not be undertaken in patients who are on corticosteroids, especially on high dose, because of possible hazards of neurological complications and a lack of antibody response.
Persons who are on drugs which suppress the immune system are more susceptible to infections than healthy individuals. Chickenpox and measles, for example, can have a more serious or even fatal course in non-immune children or adults on corticosteroids. In such children or adults who have not had these diseases, particular care should be taken to avoid exposure. How the dose, route and duration of corticosteroid administration affects the risk of developing a disseminated infection is not known. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known. If exposed to chickenpox, prophylaxis with varicella zoster immune globulin (VZIG) may be indicated. If exposed to measles, prophylaxis with pooled intramuscular immunoglobulin (IG) may be indicated. (See the respective package inserts for complete VZIG and IG prescribing information.) If chickenpox develops, treatment with antiviral agents may be considered.
The use of prednisone in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for management of the disease in conjunction with an appropriate antituberculous regimen.
If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur. During prolonged corticosteroid therapy, these patients should receive chemoprophylaxis.

USAGE IN PREGNANCY
Since adequate human reproduction studies have not been done with corticosteroids, the use of these drugs in pregnancy, nursing mothers or women of childbearing potential requires that the possible benefits of the drug be weighed against the potential hazards to the mother and embryo or fetus. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

PRECAUTIONS

General
Drug-induced secondary adrenocortical insufficiency may be minimized by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, hormone therapy should be reinstituted. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.

There is an enhanced effect of corticosteroids in patients with hypothyroidism and in those with cirrhosis.
Corticosteroids should be used cautiously in patients with ocular herpes simplex because of possible corneal perforation.
The lowest possible dose of corticosteroid should be used to control the condition under treatment, and when reduction in dosage is possible, the reduction should be gradual.
Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomnia, mood swings, personality changes, and severe depression, to frank psychotic manifestations. Also, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.
Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia.
Steroids should be used with caution in nonspecific ulcerative colitis, if there is a probability of impending perforation, abscess, or other pyogenic infection, diverticulitis, fresh intestinal anastomoses, active or latent peptic ulcer, renal insufficiency, hypertension, osteoporosis, and myasthenia gravis.
Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed.

Information for Patients
Persons who are on immunosuppressant doses of corticosteroids should be warned to avoid exposure to chickenpox. Patients should also be advised that if they are exposed, medical advice should be sought without delay.

ADVERSE REACTIONS
Fluid and Electrolyte Disturbances:

Sodium retention.

Fluid retention.

Congestive heart failure in susceptible patients.

Potassium loss.

Hypokalemic alkalosis.

Hypertension.

Musculoskeletal:

Muscle weakness.

Steroid myopathy.

Loss of muscle mass.

Osteoporosis.

Vertebral compression fractures.

Aseptic necrosis of femoral and humeral heads.

Pathologic fracture of long bones.

Gastrointestinal:

Peptic ulcer with possible perforation and hemorrhage.

Pancreatitis.

Abdominal distention.

Ulcerative esophagitis.

Dermatologic:

Impaired wound healing.

Thin fragile skin.

Petechiae and ecchymoses.

Facial erythema.

Increased sweating.

May suppress reactions to skin tests.

Neurological:

Convulsions.

Increased intracranial pressure with papilledema (pseudo-tumor cerebri) usually after treatment.

Vertigo.

Headache.

Endocrine:

Menstrual irregularities.

Development of cushingoid state.

Suppression of growth in children.

Secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress, as in trauma, surgery or illness.

Decreased carbohydrate tolerance.

Manifestations of latent diabetes mellitus.

Increased requirements for insulin or oral hypoglycemic agents in diabetics.

Ophthalmic:

Posterior subcapsular cataracts.

Increased intraocular pressure.

Glaucoma.

Exophthalmos.

Metabolic:

Negative nitrogen balance due to protein catabolism.

DOSAGE AND ADMINISTRATION

Dosage of prednisone should be individualized according to the severity of the disease and the response of the patient. For infants and children, the recommended dosage should be governed by the same considerations rather than strict adherence to the ratio indicated by age or body weight.

Hormone therapy is an adjunct to, and not a replacement for, conventional therapy.

Dosage should be decreased or discontinued gradually when the drug has been administered for more than a few days.

The severity, prognosis, expected duration of the disease, and the reaction of the patient to medication are primary factors in determining dosage.

If a period of spontaneous remission occurs in a chronic condition, treatment should be discontinued.

Blood pressure, body weight, routine laboratory studies, including two-hour postprandial blood glucose and serum potassium, and a chest X-ray should be obtained at regular intervals during prolonged therapy. Upper GI X-rays are desirable in patients with known or suspected peptic ulcer disease.

The initial dosage of prednisone may vary from 5 mg to 60 mg per day depending on the specific disease entity being treated. In situations of less severity lower doses will generally suffice, while in selected patients higher initial doses may be required. The initial dosage should be maintained or adjusted until a satisfactory response is noted. If after a reasonable period of time there is a lack of satisfactory clinical response, prednisone should be discontinued and the patient transferred to other appropriate therapy.

IT SHOULD BE EMPHASIZED THAT DOSAGE REQUIREMENTS ARE VARIABLE AND MUST BE INDIVIDUALIZED ON THE BASIS OF THE DISEASE UNDER TREATMENT AND THE RESPONSE OF THE PATIENT.

After a favorable response is noted, the proper maintenance dosage should be determined by decreasing the initial drug dosage in small increments at appropriate time intervals until the lowest dosage which will maintain an adequate clinical response is reached. It should be kept in mind that constant monitoring is needed in regard to drug dosage. Included in the situations which may make dosage adjustments necessary are changes in clinical status secondary to remissions or exacerbations in the disease process, the patient's

individual drug responsiveness, and the effect of patient exposure to stressful situations not directly related to the disease entity under treatment; in this latter situation, it may be necessary to increase the dosage of prednisone for a period of time consistent with the patient's condition. If after long-term therapy the drug is to be stopped, it recommended that it be withdrawn gradually rather than abruptly.

HOW SUPPLIED

PrediSONE Tablets USP

1 mg white, scored tablets (identified 54 092).

NDC 0054-8739-25: Unit dose, 10 tablets per strip, 10 strips per shelf pack, 10 shelf packs per shipper.
NDC 0054-4741-25: Bottles of 100 tablets.
NDC 0054-4741-31: Bottles of 1000 tablets.

2.5 mg white, scored tablets (Identified 54 339)

NDC 0054-8740-25: Unit dose, 10 tablets per strip, 10 strips per shelf pack, 10 shelf packs per shipper.
NDC 0054-4742-25: Bottles of 100 tablets.

5 mg white, scored tablets (Identified 54 612).

NDC 0054-8724-25: Unit dose, 10 tablets per strip, 10 strips per shelf pack, 10 shelf packs per shipper.
NDC 0054-4728-25: Bottles of 100 tablets.
NDC 0054-4728-31: Bottles of 1000 tablets.

10 mg white, scored tablets (Identified 54 899).

NDC 0054-0017-20: Unit dose, 10 tablets per strip, 10 strips per shelf pack, 10 shelf packs per shipper.
NDC 0054-0017-25: Bottles of 100 tablets.
NDC 0054-0017-29: Bottles of 500 tablets.

20 mg white, scored tablets (Identified 54 760).

NDC 0054-0018-20: Unit dose, 10 tablets per strip, 10 strips per shelf pack, 10 shelf packs per shipper.
NDC 0054-0018-25: Bottles of 100 tablets.
NDC 0054-0018-29: Bottles of 500 tablets.

50 mg white, scored tablets (Identified 54 343).

NDC 0054-0019-20: Unit dose, 10 tablets per strip, 10 strips per shelf pack, 10 shelf packs per shipper.
NDC 0054-0019-25: Bottles of 100 tablets.

Storage and Dispense

Store at 25°C (77°F), excursions permitted to 15° to 30°C [see USP Controlled Room Temperature]. Dispense in a tight container, as defined in the USP/NF.

PrediSONE Oral Solution

5 mg per 5 mL Oral Solution.

NDC 0054-8722-16: Unit dose Patient Cup™ filled to deliver 5 mL (5 mg Prednisone), ten 5 mL Patient Cups™ per shelf pack, 4 shelf packs per shipper.
NDC 0054-3722-50: Bottles of 120 mL.
NDC 0054-3722-63: Bottles of 500 mL.

Storage and Dispense

Store at 25°C (77°F), excursions permitted to 15° to 30°C [see USP Controlled Room Temperature]. Dispense in a tight container, as defined in the USP/NF.

PrediSONE *Intensol*™

5 mg per mL Intensol™.

NDC 0054-3721-44: Bottles of 30 mL with calibrated dropper (graduations of 0.25 mL to 1.0 mL on the dropper).

Storage and Dispense

Store at 25°C (77°F), excursions permitted to 15° to 30°C [see USP Controlled Room Temperature]. Dispense in a tight, light-resistant container, as defined in the USP/NF. Discard opened bottle after 90 days.

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Boehringer Ingelheim
Roxane Laboratories